EFFECT OF FLUID COUNTERMEASURES OF VARYING OSMOLARITY ON CARDIOVASCULAR RESPONSES TO ORTHOSTATIC STRESS

Final Report

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ABSTRACT

Current operational procedures for shuttle crewmembers includes the ingestion of a fluid countermeasure approximately 2 hours before reentry into the earth's gravitational field. The ingestion of the fluid countermeasure is thought to restore plasma volume and improve orthostatic responses upon reentry. The present countermeasure consists of ingesting salt tablets and water to achieve an isotonic solution. It has yet to be determined whether this is the optimal drink to restore orthostatic tolerance. It is also not known whether the drink solution is effective in increasing plasma volume. The purpose of this study was evaluate the effectiveness of drink solutions of different osmolarity on restoring plasma volume and orthostatic responses. Six men (age = 31 $\pm$ 3.5 yrs, weight = 80.2 $\pm$ 4.7 kg, height = 179.8 $\pm$ 2.6 cm) were tested after giving informed consent and a medical screening. Each subject participated in four conditions. In all four conditions lower body negative pressure (LBNP) was used to test orthostatic responses. In the first condition, orthostatic responses were tested after no change in hydration state of the subject (euhydrated). In the second condition, the subject was dehydrated with lasix administration (20 mg IV). This was done to simulate the loss of plasma volume during spaceflight. In a third condition, orthostatic responses were tested following dehydration and rehydration with an isotonic countermeasure (1 liter of .9% saline). In the final condition, a hyperosmotic drink solution (1 liter of 1.07% saline) was given after lasix dehydration. Plasma volume, leg circumference, plasma osmolarity, forearm blood flow, heart rate, stroke volume, blood pressure, thoracic fluid index, and cardiac dimensions (echocardiography) were measured during rest, LBNP exposure, and recovery. Subjects lost approximately 12% of the initial plasma volume (420 ml) as a result of dehydration with lasix. Rehydration with the isotonic solution partially restored plasma volume, whereas the hypertonic drink solution fully restored plasma volume back to the euhydrated level. Thoracic fluid index (TFI) increased during LBNP in all conditions. However, the starting level of TFI were different, reflecting the differences in plasma volume. This suggests that there was a greater central blood volume during the euhydrated and hypertonic conditions than in the dehydrated and isotonic conditions. Even though there were differences in plasma volume and TFI, there were few differences in any other responses measured. Heart rate was slightly elevated during the dehydrated condition relative to the other three conditions. Stroke volume, systolic and diastolic blood pressure, forearm blood flow, and leg circumference were not different between conditions. The 12% reduction in plasma volume observed in this study was not sufficient to produce profound differences in the cardiovascular responses to orthostatic stress. This suggests that other mechanisms might be operational in producing the orthostatic intolerance following short duration space flight.

INTRODUCTION

Orthostatic hypotension has been commonly reported after space flight by crewmembers both during reentry and upon egress from a spacecraft. The decrease in blood pressure could have severe ramifications on the ability of the crew to control the spacecraft during reentry and any emergency egress that might occur. Orthostatic intolerance after short duration space flight (5-14 days) is thought to be a result of a reduction in plasma volume.

Plasma volume decreases during spaceflight as a result of a negative water balance. The decrease in plasma volume has been reported to be between 8 and 15% (8). In microgravity, there is a redistribution of fluids from the lower body to the head and upper body. Originally this was thought to result in a suppression of antidiuretic hormone and a potentiated diuresis (7). Recent studies have suggested that atrial natriuretic factor (ANF) is involved in the control of plasma volume during volume expansion (9,10). It is possible that ANF is involved in plasma volume regulation during space flight.

Crew members are well suited to a microgravity environment. However, upon return to a gravitational environment they are hypovolemic relative to preflight and thus more prone to orthostatic intolerance. A study by Bungo and Charles(1) has indicated that fluid ingestion prior to reentry minimizes the impairment of orthostatic responses following spaceflight. They attribute the improvement in orthostatic responses in those crewmembers that ingested a fluid countermeasure to a restoration of plasma volume as a direct result of the ingestion of the solution. No controlled measurements of plasma volume with and without the countermeasure have ever been made.

The present countermeasure consists of ingesting salt tablets and eight ounces of water approximately 2 hours before reentry. This is thought to result in an isotonic solution (.9% saline). A recent study by Bungo et al. (2) has looked at the ingestion of drinks of varying osmolarity and composition on plasma volume. They found that a hypertonic drink solution was more effective in increasing and maintaining plasma volume (4 hours).

To date, no studies have looked at the relationship between plasma volume and LBNP tolerance in a controlled study. The purpose of this study was to evaluate the effectiveness of drink solutions of varying osmolarity on restoring plasma volume and orthostatic responses.

HISTORICAL BACKGROUND

For a detailed historical background, please see 1988 Summer Faculty Fellowship Report (4).

METHODS

Six volunteers were recruited for the study by Krug International. All subjects were medically screened and given a detailed explanation of the study. Informed consent was obtained from all subjects before participating in the study. The study was approved by the JSC IRB. Each subject participated in four conditions: 1) LBNP control - euhydrated (EUH), 2) LBNP following lasix dehydration (DEH), 3) LBNP following lasix dehydration (20 mg IV) and rehydration (ISO) with an isotonic drink solution (1 liter of a .9% saline solution), and 4) LBNP following dehydration with lasix and rehydration (HYPER) with a hypertonic drink (1 liter of a 1.07% saline solution). Control LBNP tests were administered to each subject until a consistent pattern of responses was produced. Lasix was used to simulate the decrease in plasma volume observed during spaceflight. This dosage of lasix produced approximately a 12% reduction in plasma volume from the euhydrated level as has been reported previously (4). We randomized the order of treatments to eliminate any effects of one LBNP test on a subsequent test. All experiments began at the same time of day for each individual subject to eliminate any circadian effects on our findings. Testing began 2 hours after the ingestion of a small meal. Lower body negative pressure was performed approximately 3 hours and 30 minutes after ingestion of fluids. At least 72 hours was allowed between testing sessions.

Lower body negative pressure was applied using a chamber sealed at the waist with a rubber gasket. A vacuum pump was then used to withdraw air out of the chamber. The LBNP protocol is displayed in Table 1. The test was terminated if the subject's systolic blood pressure dropped suddenly (greater than 25 mmHg in 1 minute), systolic pressure reached 80 mmHg, bradycardia occurred (drop in HR greater than 15 BPM), subject distress, or subject request. Before, during, and immediately after LBNP a series of physiological measures described below were determined every minute. Only the results from the last 3 minutes from each stage were analyzed as the first 2 minutes at each stage represent transition responses.

Table 1. LBNP protocol

Time at Stage (min)	Pressure (mmHg)
20	0
5	-5
5	-10
5	-20
5	-30
5	-40
5	-50
5	0

Blood samples were taken from an antecubital vein before lasix injection (baseline) after lasix injection, after drink ingestion, 2 and 1/2 hours after drink ingestion, 90 minutes before, and immediately after LBNP. Changes in plasma volume were calculated from hematocrit (microhematocrit technique) and hemoglobin (Coulter Counter) ratios using the formula of Dill and Costill (5). A direct measurement of plasma volume was performed once (human serum labeled 125-I) in each subject before the first experimental testing. This value was used as the absolute plasma volume and changes were expressed relative to that value. Plasma osmolality was determined using freezing point depression on all blood samples. A 5 ml sample was required to do all of the hematological analysis. Plasma levels of antidiuretic hormone, atrial natriuretic factor, aldosterone, and catecholamines (epinephrine, norepinephrine) were measured for certain blood samples.

Leg circumference measurements were made every minute with a mercury-in-silastic strain gauge. The changes in leg circumference during LBNP exposure were used to approximate the amount of venous pooling in the legs.

Venous occlusion plethysmography with a mercury-in-silastic strain gauge was used to measure forearm blood flow. The forearm vasoconstrictor response as indicated by this technique was measured at each step of LBNP. Heart rate was determined using a three lead EKG. Blood pressure was measured once a minute using a standard auscultatory technique. 2-D and M-Mode echocardiography (ATL 4000 S/LC ultrasound system, ATL, Botheli, WA.) was performed at each stage of LBNP in order to assess relative changes in left ventricular dimensions with LBNP. Thoracic fluid index and stroke volume were measured with bioelectrical impedance (BOMED). Thoracic fluid index represents the impedance to current flow and thus is inversely related to the amount of fluid in the chest.

EMG was used to assess abdominal and leg muscle tension in order to monitor for muscle tensing. The subject was asked to maintain a resting EMG level throughout all LBNP tests.

RESULTS

Plasma Volume and Plasma Osmolarity.

Plasma volume decreased by approximately 12% as a result of lasix injection (Figure 1). Drink ingestion with the isotonic drink solution partially restored plasma volume to euhydrated levels. Ingestion of the hypertonic drink solution (HYPER) fully restored plasma volume to euhydrated levels. Plasma osmolarity did not change through any of the dehydration or rehydration procedures (Figure 2). This indicates the fluid losses and gains were isotonic relative to the plasma. There was a slight increase in plasma volume in all four conditions from the post drink to the pre

LBNP sample. This was probably a result of a change in posture (sitting to supine). During LBNP there was a decrease in plasma volume in all four conditions. This hemoconcentration has been commonly observed in the literature.

Thoracic Fluid Index.

Thoracic fluid index (TFI) increased in all four conditions with increasing levels of LBNP (Figure 3). This represents an increase in blood pooling in the legs and less in the thorax. The starting TFI was also different between condition, reflecting the different plasma volumes at the start of LBNP.

Heart Rate and Stroke Volume.

Heart rate increased in all conditions with increasing levels of LBNP (Figure 4). Heart rates tended to be higher at the higher levels of LBNP in the dehydrated condition than in the euhydrated, isotonic, or hypertonic conditions. Stroke volume decreased with increasing LBNP (Figure 5). Even though plasma volume and TFI were different between the conditions, stroke volumes were similar in the four conditions.

Blood Pressure.

Systolic blood pressure decreased with increasing levels of LBNP (Figure 6). However, there were no differences in systolic blood pressure between conditions. Diastolic pressure tended to increase at the higher levels of LBNP in the dehydrated, isotonic, and hyperhydrated conditions (Figure 7). There were no differences in mean arterial blood pressure with increasing LBNP stage or between conditions.

Forearm Blood Flow and Leg Circumference.

Forearm blood flow decreased in all conditions with increasing levels of LBNP (Figure 8). This was a reflex response to maintain blood pressure in the face of falling venous return. There were no differences between conditions. Leg circumference increased with increasing levels of LBNP (Figure 9). As LBNP level increases, venous pooling in the legs increase. There were no differences in leg circumference with differing hydration states.

DISCUSSION

Lasix reduced plasma volume by 12% in the present study. This was similar to the reduction observed in our previous study (4). Rehydration with an isotonic solution (present operational countermeasure) partially restored plasma volume to the euhydrated level. When subjects ingested the hypertonic solution, plasma volume was fully restored to the euhydrated level. These data support a recent study (2) which demonstrated that plasma volume increased following ingestion of both an isotonic and hypertonic drink solution, but the plasma volume was maintained longer with the hypertonic solution.

Bungo and Charles (1) found that ingestion of a drink solution improved orthostatic tolerance after spaceflight. They attributed the decrease in orthostatic tolerance (higher heart rates, lower blood pressures) to the decrease in plasma volume that has been observed after space flight (8). We expected to see improved orthostatic responses after rehydration with both the isotonic and hypertonic drink solutions in comparison to the dehydrated condition, our model for space flight. However, there were only minor differences between conditions in heart rate, stroke volume,blood pressure (systolic and diastolic), forearm blood flow, and leg circumference.

It is possible that the differences in plasma volume produced in this study were not great enough to produce marked differences in cardiovascular responses. Other studies using exercise as a stressor have shown that plasma volume differences of the magnitude observed in this study produce significant differences in cardiovascular responses (6).

It is also possible that the reduction in plasma volume produced by lasix administration does not truly model spaceflight. Lasix did produce a 12% reduction in plasma volume which is consistent with space flight reductions in plasma volume. Our model might not have produce some of the other physiological alterations that have been observed with space flight. However, most of the alterations that would influence orthostatic responses are thought to occur in response to longer duration space flight (greater than 14 days). Although a recent study by Convertino et al. (3) has demonstrated changes in venous compliance with 4 days of 6° head down bed rest. This reduction in venous compliance was inversely related to the loss of the size of the leg muscle compartment. This might be a contributing factor to the orthostatic intolerance that occurs after short duration spaceflight and might be more important than plasma volume alterations.

Another explanation could be the difference in the composition of the countermeasure. The present countermeasure consists of ingesting 2 salt tablets and 8 ounces of water every 30 minutes for 2 hours prior to reentry. In the present study, subjects ingested a solution of .9% saline. Perhaps there are differences in the physiological effects of ingesting a solution verses salt tablets and water.

CONCLUSIONS

A hypertonic drink solution was more effective in restoring plasma volume after dehydration than an isotonic solution. However, there were no differences in their effects on an orthostatic challenge. These data suggest that the plasma volume differences produced in this study were not sufficient to produce differences in the cardiovascular responses to an orthostatic challenge, or there are other changes that occur during space flight that are more important in determining orthostatic intolerance.

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Figure 1. Plasma volume plotted as a function of sample number. Mean + SE

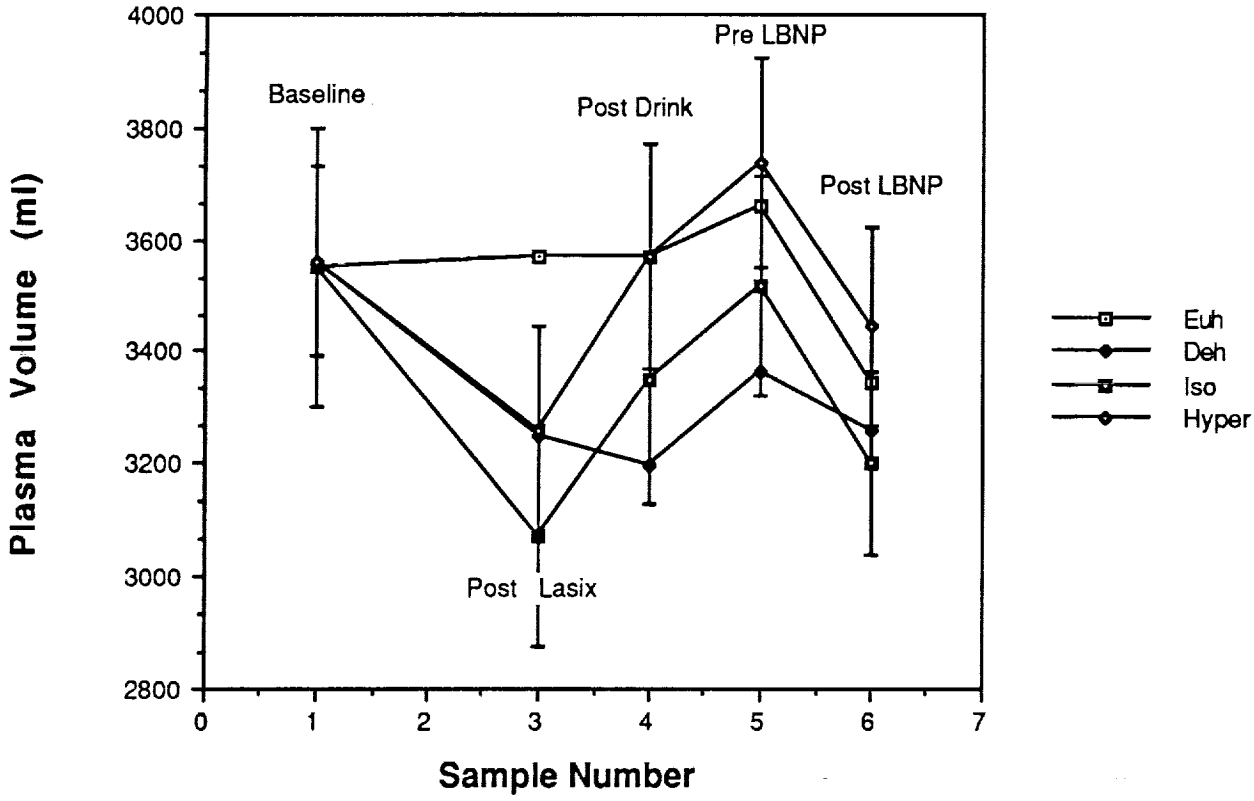

Figure 2. Plasma Osmolarity plotted as a function of sample number. Mean + SE

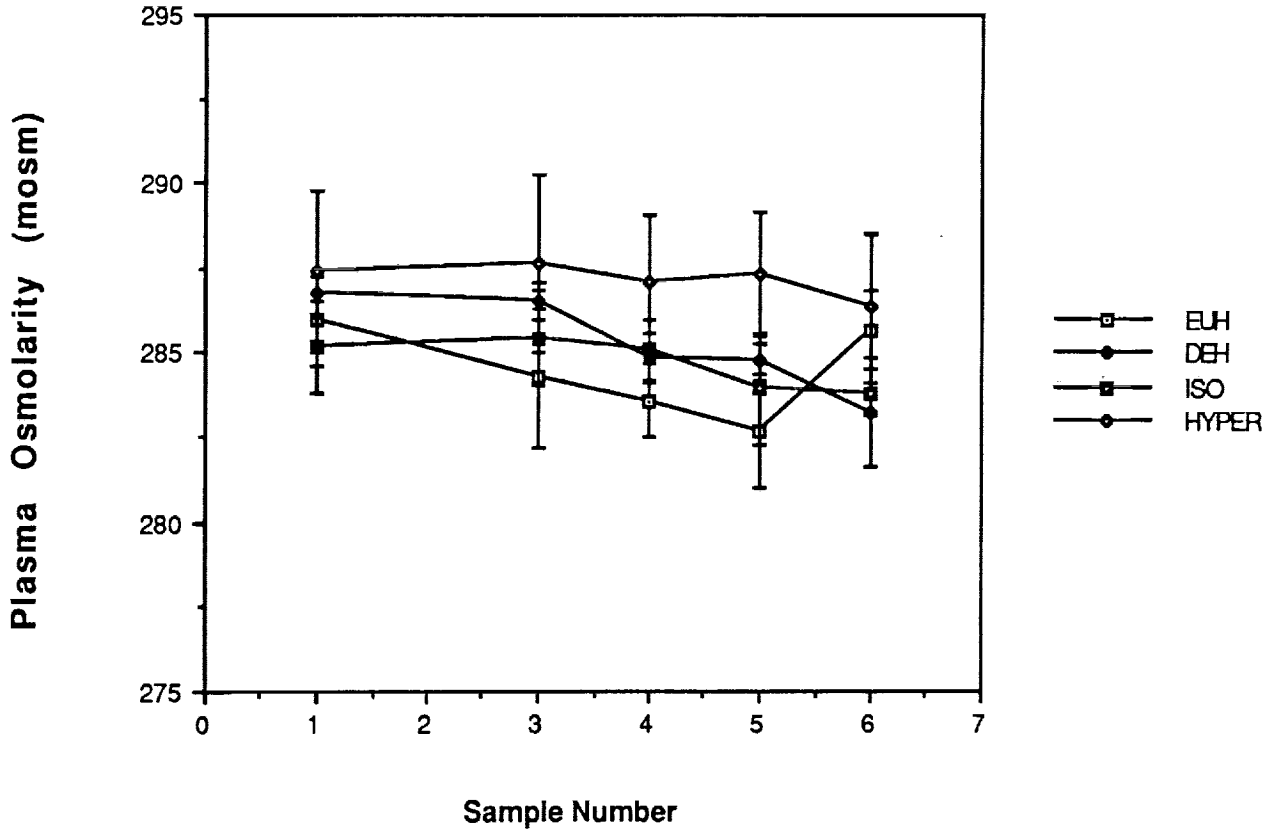

Figure 3. Thoracic fluid index plotted as a function of LBNP stage. Mean + SE.

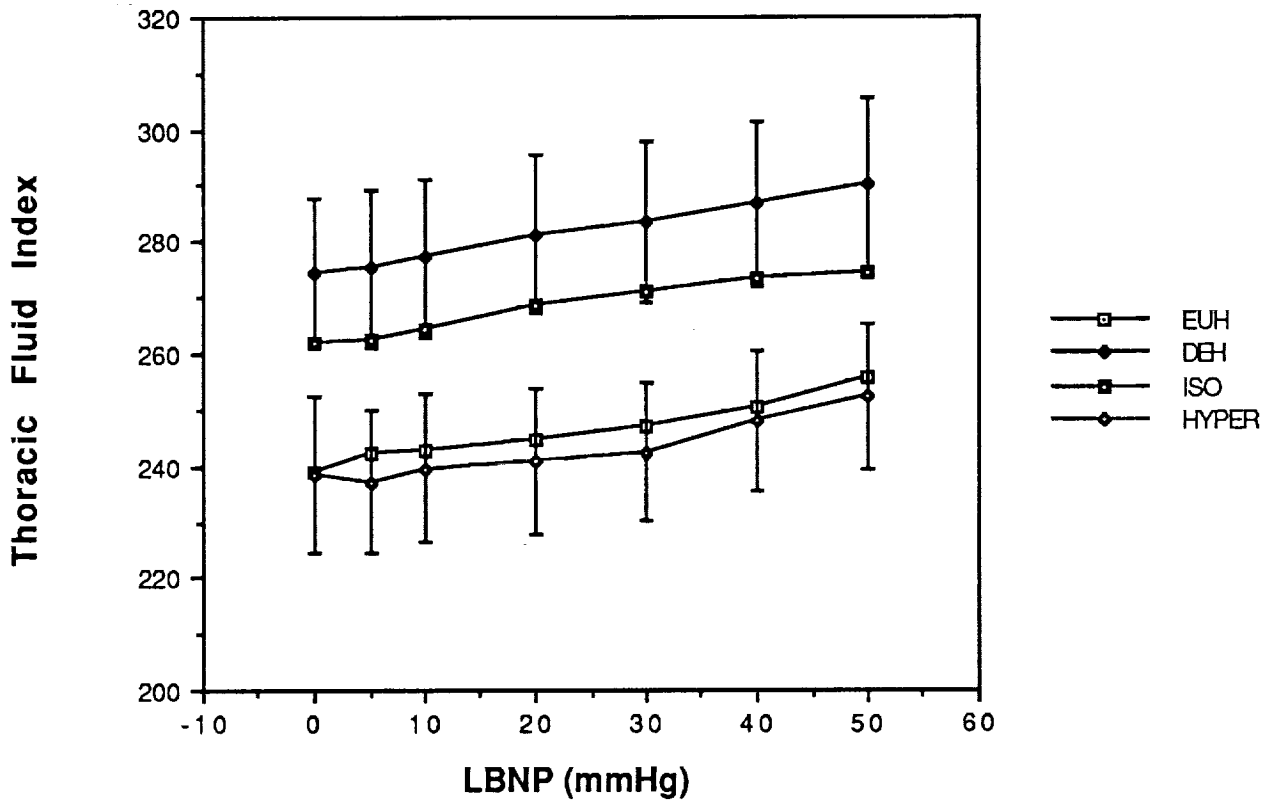

Figure 4. Heart rate plotted as a function of LBNP stage. Mean + SE.

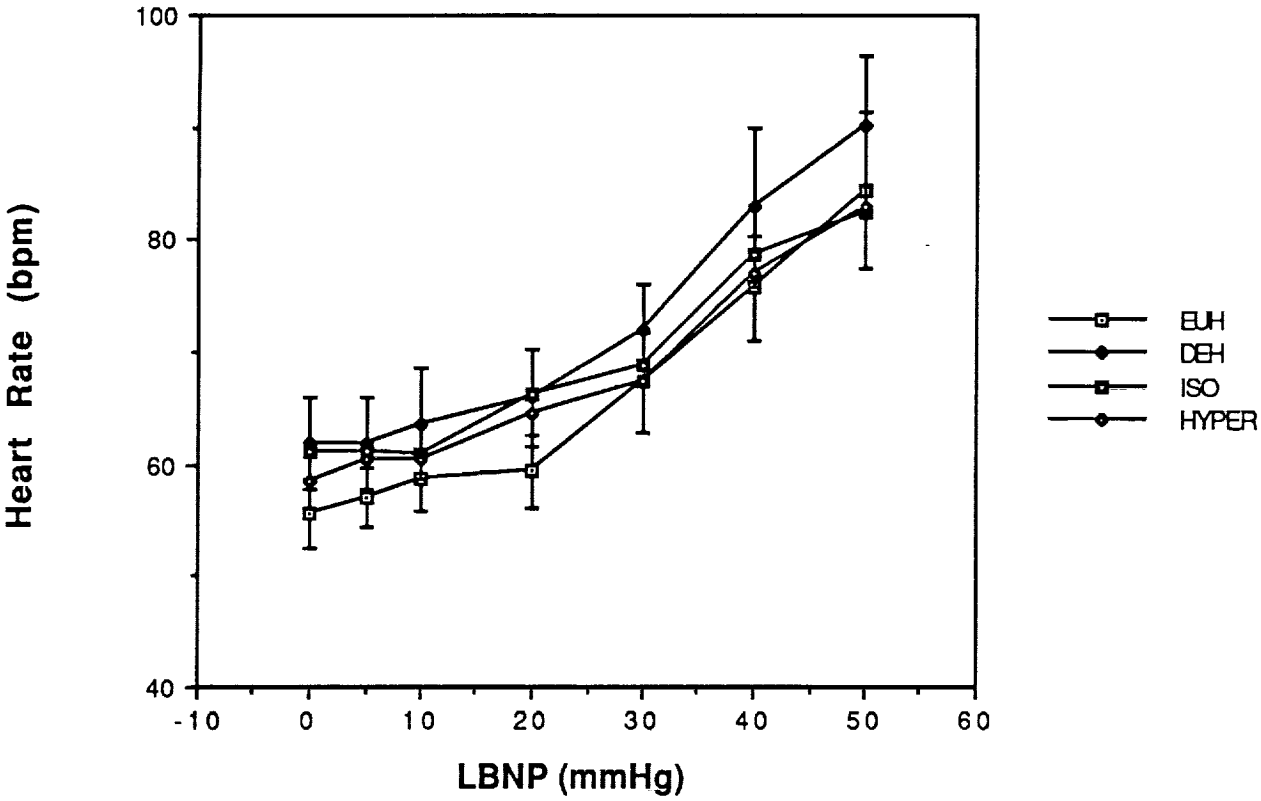

Figure 5. Stroke volume plotted as a function of LBNP stage. Mean + SE.

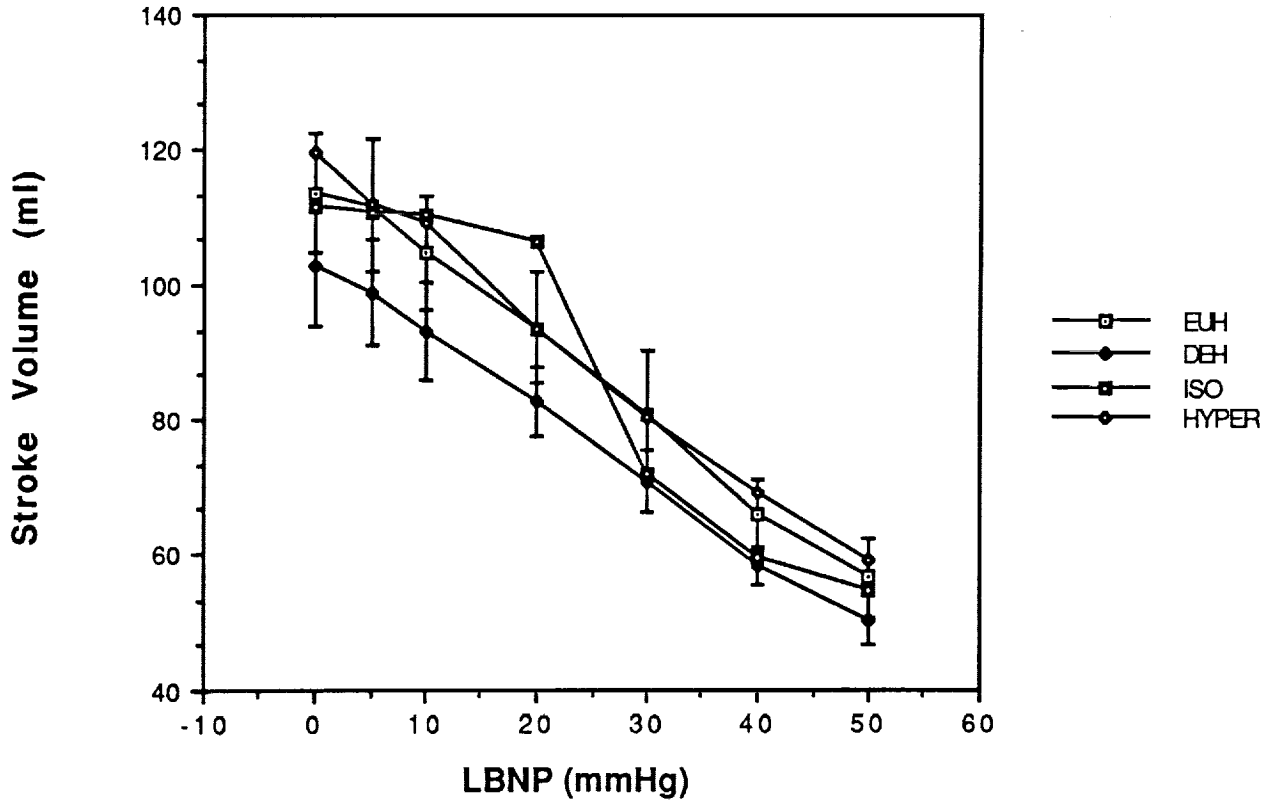

Figure 6. Systolic Blood Pressure plotted as a function of LBNP stage. Mean + SE.

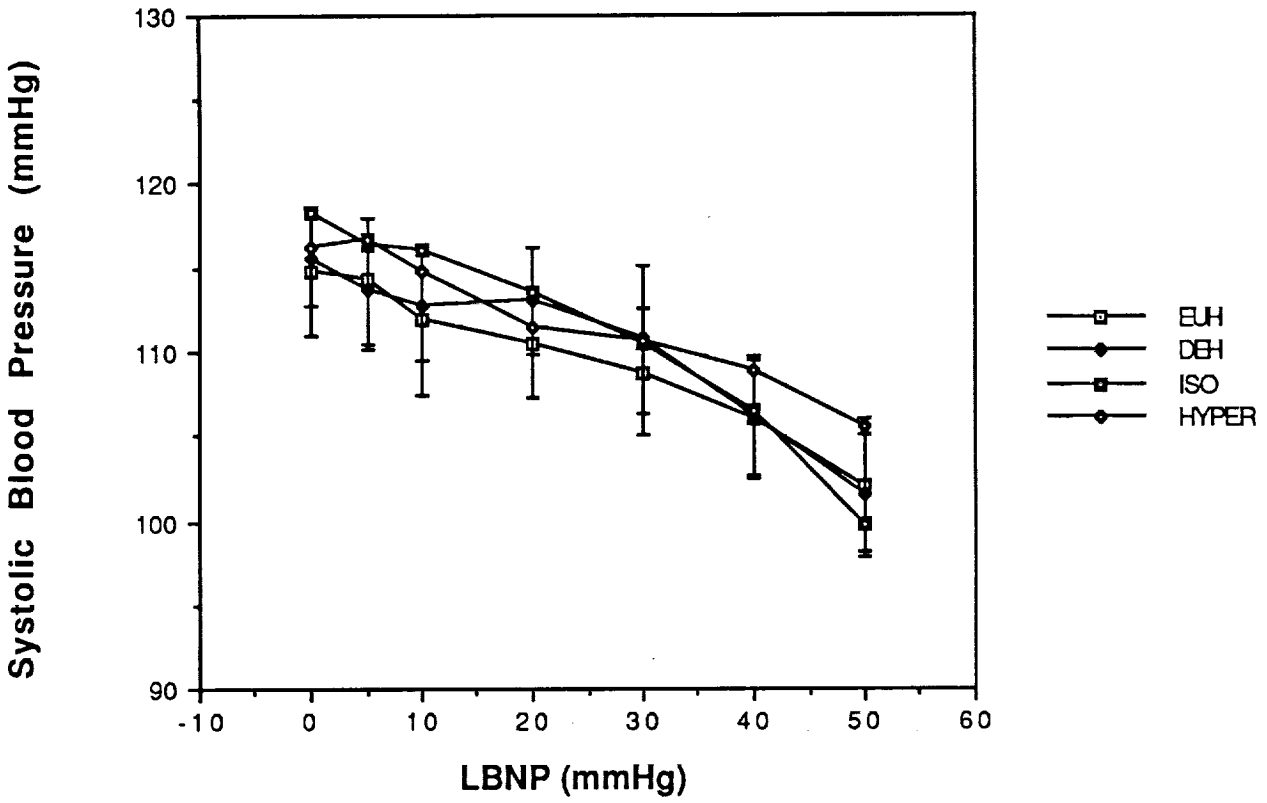

Figure 7. Diastolic blood presure plotted as a function of LBNP stage. Mean +SE.

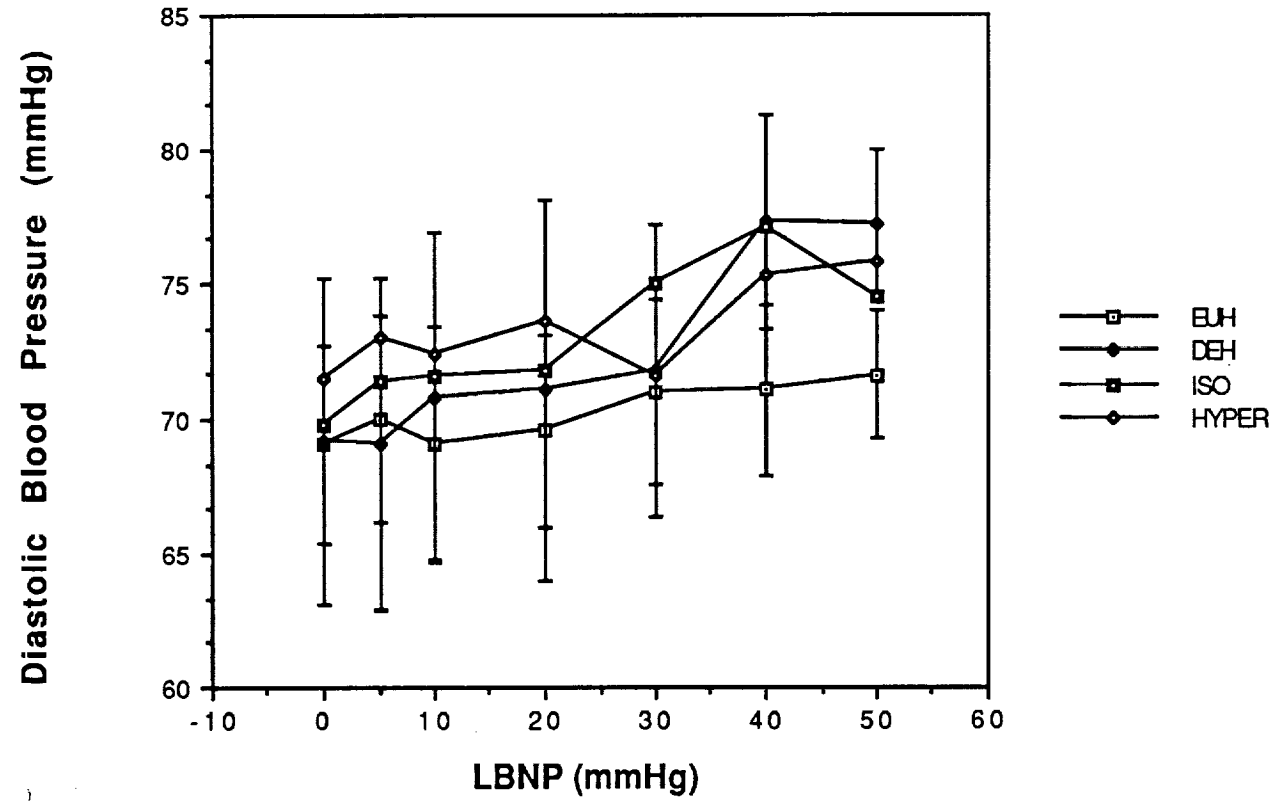

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Figure 8. Forearm blood flow plotted as a function of LBNP stage. Mean + SE.

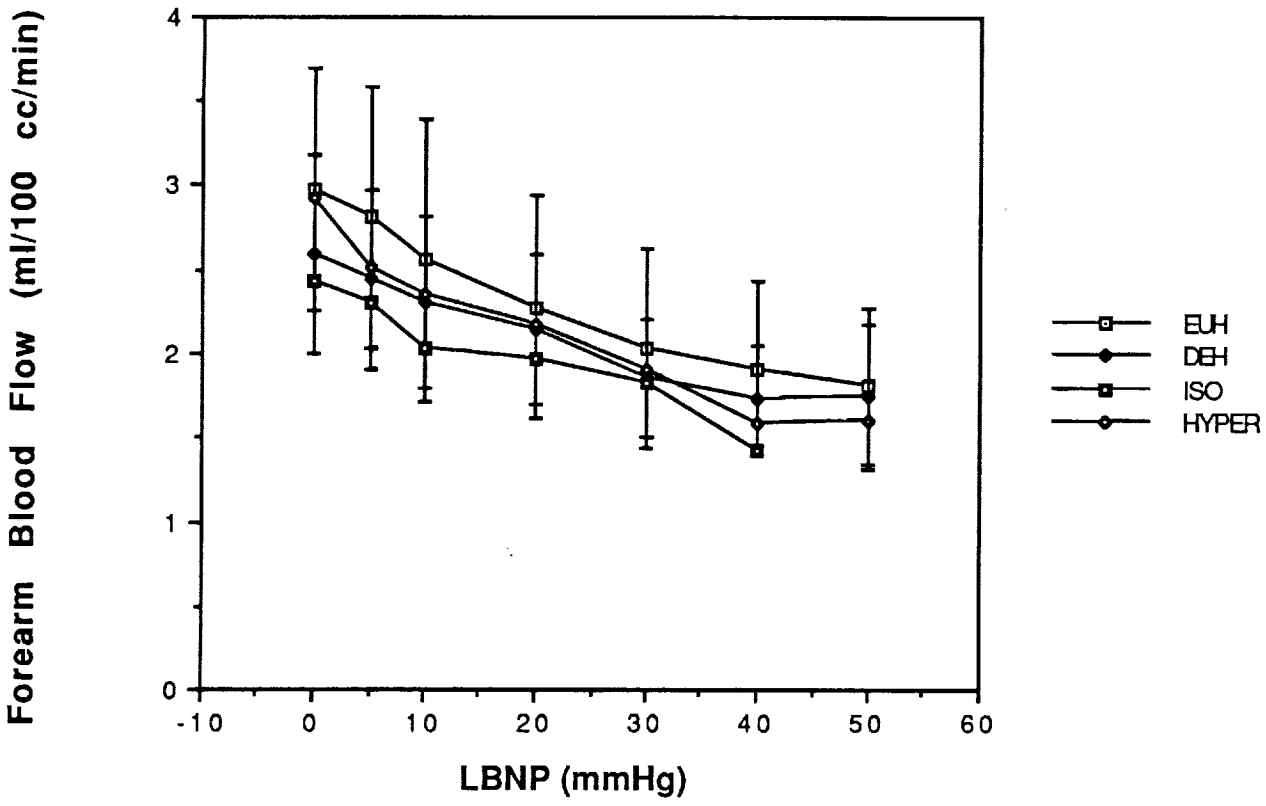

Figure 9. Change in leg circumference plotted as a function of LBNP stage. Mean + SE.